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Chronic kidney disease management in the United Kingdom: NEOERICA project results

PE Stevens[1], DJ O'Donoghue[2], S de Lusignan[3], J Van Vlymen[4], B Klebe[5], R Middleton[2], N Hague[6], J New[7] and CKT Farmer[1]

[1]Department of Renal Medicine, East Kent Hospitals NHS Trust, Kent and Canterbury Hospital, Ethelbert Road, Canterbury, Kent, UK; [2]Department of Renal Medicine, Salford Royal Hospitals NHS Trust, Hope Hospital, Salford, UK; [3]Primary Care Informatics, Division of Community Health Sciences, St George's – University of London, London, UK; [4]Primary Care Informatics, Division of Community Health Sciences, St George's – University of London, London, UK; [5]Department of Renal Medicine, East Kent Hospitals NHS Trust, Kent and Canterbury Hospital, Ethelbert Road, Canterbury, Kent, UK; [6]Primary Care Informatics, Division of Community Health Sciences, St George's – University of London, London, UK; [7]Department of Diabetes, Salford Royal Hospitals NHS Trust, Hope Hospital, Salford, UK

Early identification of patients with chronic kidney disease (CKD) may allow health-care systems to implement interventions aimed at decreasing disease progression and eventual morbidity and mortality. Primary care in the United Kingdom is computerized suggesting a separate screening program for CKD may not be necessary because identifying data already populates primary care databases. Our study utilized a data set of 163 demographic, laboratory, diagnosis, and prescription variables from 130 226 adults in the regions of Kent, Manchester, and Surrey. The patients were 18 years of age and older in a 5-year study period culminating in November 2003. Estimated glomerular filtration rate was calculated from the four-variable Modification of Diet in Renal Disease equation using calibrated creatinine levels. A valid creatinine value was recorded in almost 30% of this cohort. The age-standardized prevalence of stage 3–5 CKD was 10.6% for females and 5.8% for males. In these patients, the odds ratio for hypertension was 2.1, for diabetes 1.33, and for cardiovascular disease 1.69. Only 20% of the diabetic people with stage 3–5 CKD had a blood pressure less than or equal to 130/80 mm Hg. The proportion of patients with anemia significantly rose as renal function declined. We suggest that stage 3–5 CKD is easily detected in existing computerized records. The associated comorbidity and management is readily available enabling intervention and targeting of specialist resources.

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KEYWORDS: cardiovascular disease; chronic kidney disease; computerized medical record; estimated glomerular filtration rate; hypertension; medicines management

Correspondence: *PE Stevens, Department of Renal Medicine, East Kent Hospitals NHS Trust, Kent and Canterbury Hospital, Ethelbert Road, Canterbury, Kent CT1 3NG, UK. E-mail: paul.stevens@ekht.nhs.uk*

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Chronic kidney disease (CKD) is a major public health problem imposing a substantial burden on the patients affected and on the health-care systems caring for them. CKD is now conventionally divided into five stages (Table 1) following the classification proposed by the National Kidney Foundation Kidney Disease Outcome Quality Initiative in 2002.[1] Data from the third National Health and Nutrition Examination Survey (NHANES III) demonstrated that the number of people affected in the United States of America is high[2] and subsequent reports have detailed similar, or higher, estimates of prevalence from various countries.[3–7] The prevalence of CKD increases exponentially with age, and we can expect numbers to rise as the population continues to age and the prevalence of type II diabetes increases. Cohort studies indicate that the risk of mortality in CKD far outweighs the risk of progression to end-stage renal disease. Cardiovascular causes account for nearly 50% of the mortality and CKD is an independent predictor of cardiovascular comorbidity.[3,4,8–11]

Modeling based on NHANES data suggests that whole population screening for CKD is not a cost-effective strategy.[12] This paper describes the extent to which patients with CKD are already known to primary care in the UK but may not have been recognized as such or optimally managed. Screening of at risk populations has been shown to be effective in recognizing undiagnosed CKD.[13] Primary care physicians in the UK may already be targeting at risk populations for serum creatinine estimation such as people with diabetes or hypertension. Laboratory reporting of estimated glomerular filtration rate (eGFR) from serum creatinine has been demonstrated to improve recognition of CKD.[14] Early identification of patients with CKD may allow implementation of multiple risk factor intervention strategies aimed at reducing morbidity, mortality, and disease progression. However, this has yet to be proven and we have yet to identify a comprehensive, cost-effective means of identifying patients with CKD at an early enough stage. Primary care in the UK is now universally computerized, many practices

Table 1 | National Kidney Foundation KDOQI staging for CKD

Stage of CKD	Description	GFR (ml/min/1.73 m^2)
1	Kidney damage with normal or raised GFR	>90
2	Kidney damage with mildly reduced GFR	60–89
3	Moderately reduced GFR	30–59
4	Severe reduction in GFR	15–29
5	Kidney failure	<15

CKD, chronic kidney disease; GFR, glomerular filtration rate; KDOQI, Kidney Dialysis Outcomes Quality Initiative.

receive pathology results electronically and the majority of patient encounters are recorded electronically.

Our hypothesis was that a separate screening program for CKD may not be necessary because the data required for early identification of people with CKD and associated comorbidities already exists electronically in primary care computer databases. We explored this hypothesis by initiating a program of research under the acronym NEOERICA (NEw Opportunities for Early Renal Intervention by Computerised Assessment). We have already demonstrated the feasibility and validity of this approach.[15,16] In the first of these publications, we described prevalence and risk factor recording in 112 215 patients of all ages and confirmed that we can identify patients with CKD from primary care computer records.

This study adds to our earlier study by including a larger adult study population; calibrating creatinine before estimation of GFR; reporting the level of control of cardiovascular risk factors; and the comorbidity and current management of CKD.

RESULTS

Practice population demographics (Figure 1)

The total practice population was 162 113 with a mean age of 39.9 ± 22.6 years. Female to male ratio was 0.91:1. The population was similar to that of England and Wales in terms of age and sex profile; however, persons aged >75 years were overrepresented (Figure 2). The number aged ⩾18 years was 130 226, mean age 47.2 ± 18.78 years, female to male ratio 1:1. Only 0.63% (818/130 226) of patients had ethnicity recorded. The mean body mass index in those with both height and weight recorded was 25.8 ± 5.22 kg/m^2.

Demographics of study population (adults with a valid serum creatinine between 1 December 1998 and 30 November 2003, *n* = 38 262)

The mean age was 58.1 ± 18.1 years, and female to male ratio was 1.3:1. Height was recorded in 76.1% of the creatinine subset and weight in 80.8%, the mean body mass index was 27.1 ± 5.5 kg/m^2, (Figure 1). In the most recent 24 months of the 5-year period, 70% of the study population had an serum creatinine (SCr) recorded.

Renal function, recording of clinically relevant data, and prevalence of CKD stage 3–5

Table 2 shows the age standardized rates for CKD stage 3–5, subdivided by gender. The overall prevalence of CKD stage 3–5 was 8.5% and was higher in females, 10.6 versus 5.8% in males. The effect of creatinine standardization was to increase the proportion of those with stage 3 CKD by a factor of 1.75 and the proportion of those with stage 4 CKD by a factor of 1.6 (data not shown). The proportion of those with stage 5 CKD remained unchanged.

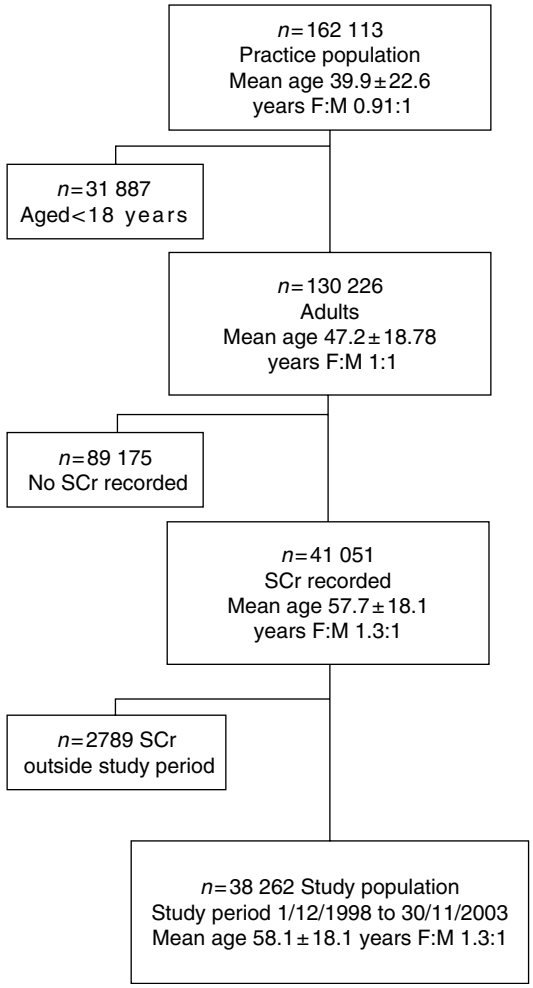

Figure 1 | Derivation of study population.

Table 3 shows the patient demographics and reported comorbidity. There was an increased female preponderance in the three strata of eGFR below 60 ml/min/1.73 m^2. In addition, the numbers of those aged ⩾70 years increased as eGFR fell; 76.7% of persons with eGFR <30 ml/min/1.73 m^2 were aged ⩾70 years.

Overall, 1.6% of the study cohort had a recording of a renal diagnosis. The proportion of patients with a recorded diagnosis of renal disease improved as renal function decreased. For the eGFR stratum <30 ml/min/1.73 m^2, 19.2% had a recorded renal diagnosis. Moreover, 27.4% had a record of hematuria/proteinuria testing.

Hemoglobin levels and anemia

Concurrent hemoglobin (Hb) levels were available in 32 385 (84.6%); (Table 4). Hb values were normally distributed in the study cohort, (mean 13.8 ± 1.5 g/dl). This was also

evident in persons with eGFR <30 ml/min/1.73 m^2, (mean 13.1 ± 1.8). The proportion of people with anemia rose across the strata of eGFR ($P<0.001$) and this was regardless of definition used to define anemia.

Using multivariate analysis, we demonstrated very little correlation between Hb and eGFR, (adjusted $R^2=0.02$). Regardless of eGFR, females were more likely to have an Hb <11 g/dl (crude odds ratio (OR) 1.69 (95% confidence interval (CI) 1.44–2.00)); age adjusted (<70 years or $\geqslant 70$ years) OR 1.63 (95% CI 1.43–1.87).

Hypertension

In the study population, blood pressure (BP) records were available in 31 740 (94.4%) of cases. 21 332 patients were defined as hypertensive by presence of hypertension read code and/or BP above 140/90 and/or on antihypertensive medication. Of these, 19 702 patients had a code for hypertension and/or BP above 140/90, and of these 9848 patients had only a hypertension read code.

Hypertension rates were similar in males and females. The crude OR for hypertension in patients with eGFR <60 ml/min/1.73 m^2 was 3.45 (3.23–3.57); age adjusted OR 2.1 (2.0–2.2). Table 5 shows the use of antihypertensive medication and achieved targets by eGFR strata. Antihypertensive use was highest in people with an eGFR <30 ml/min/1.73 m^2 (mean of 1.76 medications per person). Overall, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin 2 receptor blockers (ARBs) were used in 33.2% of people with hypertension, ACEI/ARB inhibitor use fell with decreasing eGFR ($\chi^2=452.8$, $P<0.001$). Achievement of BP targets in those with a recorded BP was relatively poor with little difference between the eGFR strata (Table 5).

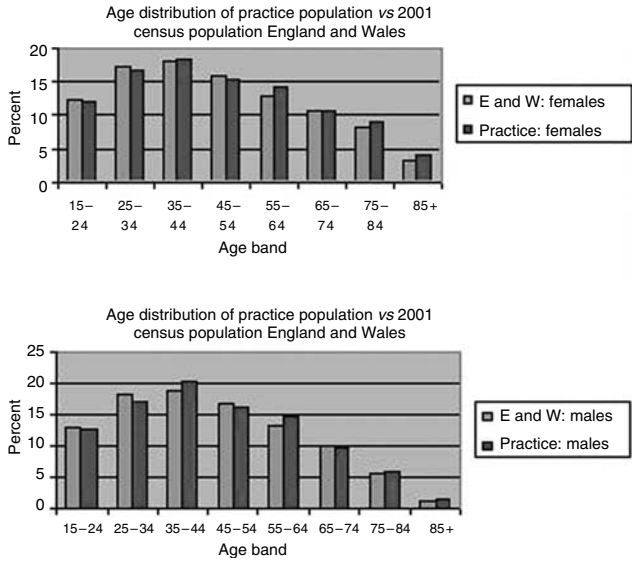

Figure 2 | Study age and sex distribution compared to England and Wales.

Diabetes mellitus

In the adult study population a diagnosis of diabetes was coded in 5058/130 226, representing an adult population prevalence of 3.9%. In the study cohort, diabetes was present in 4063/38 262 (10.6%) and prevalence increased as GFR decreased ($\chi^2=222.4$, $P<0.001$). For diabetic females, the crude OR for an eGFR <60 ml/min/1.73 m^2 was 1.85 (95% CI 1.68–2.03). This was lower in diabetic males; crude OR 1.41 (95% CI 1.28–1.56). Overall, the age/gender adjusted OR to have eGFR <60 ml/min/1.73 m^2 was 1.31 (95% CI 1.21–1.41).

In those with diabetes and eGFR <60 ml/min/1.73 m^2, ACEIs/ARBs were prescribed in 690/1601 (44%), aspirin and/or other antiplatelet agents in 621/1601 (39.6%), and lipid-lowering therapy in 942/1601 (60.1%); (Table 6). Only around one-fifth of people with an eGFR <60 ml/min/1.73 m^2 had a BP $\leqslant 130/80$ mm Hg and ACEI/ARB treatment was prescribed in 44% of cases. The proportion of diabetics

Table 2 | Age-standardized rates for stage 3–5 CKD

Age bands	Males				Females			
	Study population		*Census population		Study population		*Census population	
	n	Proportion with stage 3–5 CKD	*n*	Expected stage 3–5 CKD	*n*	Proportion with stage 3–5 CKD	*n*	Expected stage 3–5 CKD
18–24	8273	0.01%	3 671 800	443.8293	7716	0.18%	3 588 900	6511.74
25–34	12 424	0.17%	4 215 200	7 124.855	10 923	0.79%	4 259 800	33 538.7
35–44	13 115	0.71%	4 381 700	31 071.15	11 988	2.69%	4 464 600	119 920
45–54	10 566	3.08%	3 856 300	118 616.1	9973	2.79%	3 920 300	109 279
55–64	9518	6.89%	3 089 600	212 941.5	9254	13.09%	3 186 200	416 954
65–74	6356	17.65%	2 307 700	407 369.3	6943	27.86%	2 639 700	735 299
75–84	3884	33.16%	1 308 300	433 854.4	5754	41.68%	1 987 300	828 214
85+	990	44.75%	312 400	139 791.1	2549	48.61%	817 300	397 267
Total	65 126		[a]23 143 000	[b]1 351 212	65 100		[a]24 864 100	[b]2 646 984
Age-standardized rate			5.8%				10.6%	

CKD, chronic kidney disease.
*Based on UK 2001 census data.
Expected stage 3–5 CKD by age band=proportion with stage 3–5 CKD *census population.
Total for expected CKD (b)=Sum of expected CKD for age bands.
Age-standardized rate=b/a *100.

Table 3 | Demographics and recording of relevant comorbidity

	<30 ml/min/1.73 m^2 *n*=525	30–44 ml/min/ 1.73 m^2 *n*=2475	45–59 ml/min/ 1.73 m^2 *n*=8731	>60 ml/min/1.73 m^2 *n*=26 531	Total *n*=38 262
Demographics n *(%)*					
F:M	341:184	1731:744	5710:3021	13 987:12 544	21 769:16 493
	1.85:1	2.3:1	1.89:1	1.1:1	1.3:1
Aged >70 years	403 (76.7)	2009 (81.2)	4343 (49.7)	4136 (15.6)	10 890 (28.5)
Characteristics mean±*s.d.*					
Age (years)*	76.8±14.1	78.4±10.4	69.7±13.5	52.3±16.8	58.1±18.1
BMI (kg/m^2)*	27.8±6.1	27.7±5.4	27.4±5.4	26.8±5.6	27.0±5.5
SBP (mm Hg)*	141.3±20.8	142.6±20.4	138.8±18.9	131.8±18.9	134.3±19.4
DBP (mmHg)*	76.7±11.2	77.9±10.8	78.8±10	78.5±10.3	78.5±10.3
SCr (mg/dl)*	2.87±1.69	1.52±0.25	1.2±0.17	0.96±0.17	1.07±0.37
GFR*	22.5±6.4	39.3±4.0	53.6±4.2	77.7±18.8	69.6±21.3
Hb (g/dl)*	13.2±1.8	13.5±1.6	13.8±1.5	13.9±1.5	13.8±1.5
Comorbidity n *(%)*					
Diabetes	121 (23)	398 (16.1)	1049 (12)	2495 (9.4)	4063 (10.6)
Hypertension	461 (87.8)	2143 (86.6)	6235 (71.4)	12 493 (47.1)	21 332 (55.8)
All CVD	266 (50.7)	1056 (42.7)	2369 (27.1)	3929 (14.8)	7620 (19.9)
Hypercholesterolemia	231 (44)	1034 (41.8)	3751 (43)	11 ,014 (41.5)	16 030 (41.9)
Proteinuria/ haematuria	144 (27.4)	610 (24.6)	1086 (12.4)	2690 (10.1)	4800 (12.5)
Renal diagnosis	101 (19.2)	90 (3.6)	51 (0.6)	355 (1.3)	597 (1.6)
BMI	372 (70.1)	1834 (74.1)	6559 (75.1)	19 736 (74.4)	28 501 (74.5)
Blood pressure record	503 (95.8)	2422 (97.9)	8482 (97.1)	24 719 (93.2)	31 740 (94.4)

ANOVA, analysis of variance; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; GFR, glomerular filtration rate; Hb, hemoglobin; SBP, systolic blood pressure.
*P<0.001 ANOVA, excluding 'All'.
For conversion of SCr to mmol/l, multiply by 88.4.

Table 4 | Anemia: definitions and mean Hb by strata of GFR

GFR stratum	<30 ml/min/1.73 m^2	30–44 ml/min/1.73 m^2	45–59 ml/min/1.73 m^2	>60 ml/min/1.73 m^2	All
‡Hb tested	439 (83.6)	2057 (83.1)	7308 (83.7)	22 581 (85.1)	32 385 (84.6)
‡WHO anemia	127 (28.3)	379 (18.4)	948 (13.0)	3024 (13.4)	4478 (13.8)
‡KDOQI anemia	94 (21.4)	294 (14.3)	590 (8.1)	1347 (6.0)	2325 (7.2)
‡Hb<11 *g*/dl	44 (10.0)	84 (4.1)	213 (2.9)	611 (2.7)	952 (2.9)
Males	12	26	53	210	301
Females	32	58	160	401	651
*Hb males	13.5±1.9	13.9±1.6	14.1±1.5	14.3±1.5	14.2±1.5
*Hb females	12.9±1.7	13.4±1.5	13.6±1.4	13.6±1.4	13.5±1.4

ANOVA, analysis of variance; GFR, glomerular filtration rate; Hb, hemoglobin; KDOQI, Kidney Dialysis Outcomes Quality Initiative; WHO, World Health Organization.
*P<0.001 ANOVA, excluding 'All'.
‡P<0.001 χ^2.
Values are mean±s.d. where appropriate.

with a glycosylated Hb greater than 7.5% was similar in those with a eGFR <60 ml/min/1.73 m^2 compared to eGFR >60 ml/ml/1.73 m^2 (40.9 vs 44.4%).

Lipids

The proportion of people with hypercholesterolemia was similar in each GFR stratum, (Table 3). After adjustment for age and gender, the OR for hypercholesterolemia in those with eGFR <60 ml/min/1.73 m^2 was 1.09 (95% CI 0.99–1.2).

Cardiovascular disease

The proportion of people in the study cohort with cardiovascular disease (CVD) was 19.9%. CVD was more prevalent in the eGFR <30 ml/min/1.73 m^2 stratum (50.7%), (Table 3). The crude OR for CVD in persons with eGFR <60 ml/min/1.73 m^2 was 2.92 (95% CI 2.71–3.13) in females and 2.86 (95% CI 2.65–3.1) in males; age/gender adjusted OR 1.69 (95% CI 1.59–1.79). Table 7 details the prescription of ACEI/ARB, antiplatelet agents and lipid-lowering therapy in those with CVD. Those with eGFR <60 ml/min/1.73 m^2 were more likely to be prescribed ACEI/ARB and antiplatelet agents. As with the total cohort, the proportion of people with CVD treated with ACEI/ARB, lipid-lowering therapy, and antiplatelet agents decreased in the eGFR <30 ml/min/1.73 m^2 stratum (data not shown).

Table 5 | Number of antihypertensive medications and achieved targets

	<30 ml/min/1.73 m^2	30–44 ml/min/1.73 m^2	45–59 ml/min/1.73 m^2	>60 ml/min/1.73 m^2	Total
Hypertension defined	461	2143	6235	12 493	21 332
Antihypertensive medications					
None	117 (25.4)	598 (27.9)	2358 (37.8)	6530 (52.3)	9603 (45)
‡Average number of antihypertensives	1.84	1.76	1.66	1.54	1.6
Use of ACEi/ARB	150 (32.5)	804 (37.5)	2679 (43)	3467 (27.8)	7100 (33.2)
Achieved targets					
*BP<150/90 mm Hg	245 (53.1)	1174 (54.8)	3315 (53.2)	6279 (50.3)	11 013 (51.6)
*BP<140/85 mm Hg	142 (30.8)	574 (26.8)	1419 (22.8)	2228 (17.8)	4363 (20.4)
*BP<130/80 mm Hg	63 (13.7)	234 (10.9)	571 (9.2)	765 (6.1)	1633 (7.7)

BP, blood pressure; eGFR, estimated glomerular filtration.
Values are *n* (%).
‡Average number of antihypertensive medications/person on treatment in eGFR strata.
*$P<0.001$.

Table 6 | Diabetes, treatment, and renal function

	eGFR <60 ml/min/1.73 m^2 *n*=1568	eGFR ⩾60 ml/min/1.73 m^2 *n*=2495	*P*-value
ACEi/ARB	690 (44.0)	880 (35.3)	$P<0.001$
Antiplatelet agents	621 (39.6)	711 (28.5)	$P<0.001$
Lipid-lowering therapy	942 (60.1)	1445 (57.9)	NS
HbA1c>7.5%	642 (40.9)	1108 (44.4)	$P<0.05$
Treated hypertension	1313 (83.7)	1590 (63.7)	$P<0.001$
BP<130/80 mm Hg in treated hypertensives	270 (21)	281 (11.2)	$P<0.001$

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin 2 receptor blocker; BP, blood pressure; eGFR, estimated glomerular filtration; HbA1c, hemoglobin A1c; NS, not significant.
Values are *n* (%).

Table 7 | Prescribed treatment in those with cardiovascular disease

Prescribed treatment	eGFR <60 ml/min/1.73 m^2 *n*=3691	eGFR ⩾60 ml/min/1.73 m^2 *n*=3929	*P*-value
ACEi/ARBs	1520 (41.1)	1352 (34.4)	<0.001
Antiplatelet agents	1899 (51.4)	1590 (40.4)	<0.001
Lipid-lowering agents	1910 (50.7)	2038 (51.9)	NS

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin 2 receptor blocker; eGFR, estimated glomerular filtration; NS, not significant.
Values are *n* (%).

DISCUSSION

Routinely collected primary care computer records can be used to not only detect patients with CKD stages 3–5, but also to describe their comorbidity and current management. We have demonstrated in a large study population, which also included institutionalized people, that the age-standardized adult prevalence of stage 3–5 CKD is 8.5% (10.6% for females and 5.8% for males). This prevalence is based on the assumption that no untested people in the primary care population have CKD stage 3–5 and therefore inevitably underestimates its prevalence. In addition due to the study design this estimate is subject to Neyman bias contributing to the underestimate of prevalence. However, the magnitude of the effect may be less than expected because 70% of patients had a serum creatinine within the last 24 months of the study period. This is discussed in detail later in the discussion. Although because of differences in methodology comparisons with other studies need to be viewed with caution, the gender specific rate for CKD stage 3–5 in this study compares to results from a population study in Iceland[17] showing age-standardized rates of 11.55 and 4.71% for females and males, respectively. Other studies have also outlined varying prevalence rates for CKD stage 3–5. A small study from Mexico ($n=3564$) recorded a prevalence of 8.5% for stage 3–5 CKD,[6] the PREVEND study[4] from the Netherlands ($n=8459$) reported a prevalence of 5.84%, and the AusDiab study[3] from Australia ($n=11\,247$) reported the highest prevalence of stage 3–5, 11.2%. A much larger study from Northern Ireland ($n=337\,618$), published in abstract only, showed an overall population prevalence of stage 3–5 CKD of 8.0%.[18] The North American comparator is the NHANES III study ($n=15\,625$), representative of the noninstitutionalized US population, which reported that 4.7% of the population had stage 3–5 CKD.[1] The methodologies of all of these studies clearly differ to that used in our study, but these are the only ones in the literature providing population prevalence estimates in the countries quoted.

The change in prevalence engendered by creatinine standardization is significant. In our earlier, smaller study, we predicted a whole population prevalence of stage 3–5 CKD of 4.9% using unstandardized creatinine data.[2] For the same study period in those aged ⩾18 years, the age-standardized prevalence would have been 4.93% (3.16% for males, 6.86% for females). The effect of standardization of creatinine was to lower eGFR and this effect was greatest at lower creatinine levels. The proportion of those with stage 5 CKD remained unchanged, whereas the proportion of those with stage 4

CKD increased by a factor of 1.6, and by a factor of 1.75 in people with stage 3 CKD.

There are clear limitations to this cross-sectional study. Although the age and sex profile of the study population were similar to that of England and Wales, ethnicity was unreliably recorded, precluding use of a correction factor for Afro-Caribbean ethnicity in eGFR calculation by the Modification of Diet in Renal Disease (MDRD) equation. Data from the Office of National Statistics suggest that 1.35% of the study population would have been of Afro-Caribbean and 4.11% of Asian ethnicity compared to 2.85 and 4.73%, respectively, in the population of England and Wales as a whole.[19] This mitigates against a significant overestimate of lower levels of eGFRs despite the lack of recording of ethnicity in the study population.

Can we assume that we have captured all those with stage 3–5 CKD? This was a cross-sectional survey of live patients, in other words a patient whose SCr had been checked but who had subsequently died before the data collection would not have appeared in the primary care database at the time of the study (Neyman bias). This will have a significant effect given the fact that large studies have demonstrated that the risk of death in CKD is high.[8,9] In addition, when interpreting the comorbidities and management of these patients, the fact that there is an overrepresentation of survivors may impact on their estimates.

Also, a SCr value was recorded in 31.5% of the adult population and in predicting the prevalence of stage 3–5 CKD, we have assumed that those who did not have a SCr measured would not have had a GFR of <60 ml/min/1.73 m^2. Only a small proportion of patients either had a coded diagnosis of renal disease, or had tests for hematuria, and/or proteinuria recorded. This poor recording was validated by the manual search of 10 979 primary care records.[16] This suggests that a relatively small proportion of people with CKD have been identified and coded as such in primary care. This is an important observation and is an area which requires future study particularly in the United Kingdom where universal eGFR reporting by laboratories was introduced in April 2006 by the Department of Health[20] and the General Practitioner Quality and Outcomes Framework (QOF)[21] included an incentive for setting up registries of patients with CKD stage 3–5 (also in April 2006) which included BP targets for patients with CKD. The impact of these measures on the recording of renal disease will be an important area of study, and so too will be the effect of increased recognition of CKD on the management of both risk factors for progression of CKD and for associated comorbidity.

The recording of important data such as BP, diabetes, CVD, Hb, and lipids was sufficiently complete to enable us to describe the associated comorbidity. Prescription data was 100% complete, allowing us to also describe the current management of these patients.

What does the data tell us? These data clearly show an exponential increase in prevalence of stage 3–5 CKD with age and suggest that female gender is a predictor of lower level of eGFR. There is a high prevalence of hypertension in patients with eGFR <30 ml/min/1.73 m^2 (87.8%) and in patients with higher, but reduced, eGFR. Our data also tell us that very few patients achieve the level of BP control required to prevent progression of renal disease.[22] Furthermore, the management of those with higher eGFR was significantly worse than those with CKD stages 3–5. A major proportion of patients with documented hypertension received no treatment. Of those who were prescribed treatment, patients with stage 3–5 CKD were significantly more likely to be prescribed ACEIs/ARBs ($P<0.001$) and a greater proportion achieved lower levels of recorded BP ($P<0.001$ for all levels) compared with those with higher eGFR. However, those with an eGFR <30 ml/min/1.73 m^2 were less likely to receive ACEI/ARB than those with an eGFR 30–60 ml/min/1.73 m^2. This implies that an opportunity to practice preventive medicine is currently being lost. Similarly, despite the wealth of literature and national guidelines supporting and advocating the importance of control of diabetes and hypertension in patients with diabetes, the levels of diabetic control and achieved BP in patients at all levels of eGFR is suboptimal and dictates the need for improvement. Our data suggest that the potential number of patients with stage 3–5 CKD and anemia defined by Kidney Dialysis Outcomes Quality Initiative in the UK is 399 020 subjects. Although not all of these may be suitable for treatment, we know that treating low Hb improves quality of life, and observational studies suggest that lower levels of Hb are associated with increased mortality and hospitalization.

A large proportion of those patients with stage 3 CKD are over the age of 75 in our cohort. We acknowledge that use of the MDRD equation in subjects older than the population from which the equation was derived is also a further potential source of bias and that this area merits further study. Furthermore, there is currently little evidence in the elderly to support the specific use of agents to delay the progression of CKD and although modification of cardiovascular risk may have an impact in the elderly, again concrete evidence for this is lacking in the setting of CKD. The key questions to be answered are what constitutes a normal GFR in the elderly, what level of GFR is associated with adverse outcomes in the elderly, are the other determinants of adverse outcomes in CKD the same for the elderly as for younger age groups, can the risk factors for these adverse outcomes be modified by intervention, and if so are the targets the same in the elderly as for younger age groups?

Recent work from our unit demonstrated that patients with significant CKD unknown to renal services have increased levels of mortality with a standardized mortality of 34.5 in those under the age of 60.[7] Cardiovascular mortality was predominant. In this study, the prevalence of all forms of CVD was greater than the general population at all levels of eGFR but was significantly increased in those with stage 3–5 CKD. Prescription data suggested that the manage-

ment of these patients could be considerably improved upon. Although patients with stage 3–5 CKD and CVD had significantly higher prescribing rates than those with higher levels of eGFR, still only 50% were prescribed antiplatelet agents and lipid-lowering therapy, and even less were prescribed ACEIs/ARBs.

Conclusion

We have shown that it is possible to use routinely collected primary care computer data to highlight CKD stage 3–5 and to describe the associated comorbidity and current management of patients with CKD stage 3–5. This approach enables considerable numbers of patients to be highlighted who could have improved primary care management of their risk factors for progression of CKD and of their cardiovascular risk, with appropriate referral to secondary care where indicated. The next phase of this project is to develop an expert system to use this existing data to guide patients with CKD into the appropriate disease management pathway.

MATERIALS AND METHODS

Practice computer data were extracted and processed using an established methodology described in detail elsewhere.[15,16] Briefly, in 2003 using Morbidity Information Query and Export Syntax (MIQUEST), a Department of Health sponsored computer program, we extracted a retrospective dataset of 163 variables from all patients in 17 primary care practices in Kent, Greater Manchester, and West Surrey over a 13-year period 1990–2003. Kent represents a predominantly Caucasian rural population with a higher proportion of people aged over 70 years compared with the UK as a whole (13.8% vs 11.5%). Greater Manchester represents a Northern city population and West Surrey is an affluent commuter area southwest of London. Morbidity Information Query and Export Syntax allows the same searches to be run on different types of primary care databases and extracts structured or 'coded' data only. Free-text, or narrative, data cannot be searched. In a separate study, the validity of using Morbidity Information Query and Export Syntax extracted data was checked by a manual search of the practice records in a practice of 10 975 patients.[16]

From the 13-year cohort, data were analysed on adults ($\geqslant$18 years) with a valid SCr between the 1 December 1998 and 30 November 2003, these are referred to as the study cohort. Anyone who had a blood test in that period but died before 1 December 2003 will not have been included in the study group cohort (Neyman bias). The data were exported into SPSS version 12.0 for analysis. Data were cleaned by removing duplicates and by manual translation of out of range data.

Variables analyzed included demographic details, biochemical and haematological laboratory data, patient history and examination data, coded diagnoses, and prescription data. All data were recorded with the date of entry.

Estimated GFR was derived from the four-variable MDRD equation.[23] To remove systematic bias in estimated GFR,[24] we calibrated the creatinine assays used in the study. Creatinine assays used in Kent were directly calibrated to the method employed by the central laboratory used for the MDRD Study (Beckman Rate Jaffe/CX3 Synchron assay).[25] This in turn enabled indirect calibration of the other creatinine assays used in the study. For descriptive purposes, and to assess better comorbidity, patients were divided into four strata of eGFR, namely, those with eGFR <30 ml/min/1.73 m^2, eGFR 30–44 ml/min/1.73 m^2, eGFR 45–59 ml/min/1.73 m^2, and those with eGFR $\geqslant 60$ ml/min/1.73 m^2.

Comorbidities were defined as follows:

(1) Hypertension: coded diagnosis of hypertension and/or recorded systolic BP >140 mm Hg or diastolic BP >90 mm Hg and/or prescription of antihypertensive treatment.
(2) Diabetes: coded diagnosis of diabetes.
(3) Anemia was defined in three different ways:
   - World Health Organization (WHO) definition: <13 g/dl in adult males and postmenopausal females and <12 g/dl in premenopausal females and prepubertal patients).
   - Kidney Dialysis Outcomes Quality Initiative definition: <11 g/dl in premenopausal females and <12 g/dl in adult males and postmenopausal females.[17]
   - Hb cutoff <11 g/dl.
(4) Hypercholesterolemia: coded diagnosis and/or prescription of cholesterol-lowering treatment and/or a total cholesterol >5 mmol/l and total cholesterol/high-density lipoprotein-cholesterol ratio of >3.0.
(5) CVD: coded diagnosis of ischemic heart disease, peripheral vascular disease, cardiac failure, and cerebrovascular disease.

Categorical data were summarized by counts and percentages. Normally distributed continuous variables were summarized by mean and s.d., nonparametric data by median values. For CKD stage 3–5 prevalence, the study cohort was subdivided into 10-year age bands. Data were age-standardized according to population rates from the UK 2001 census. To assess comorbidity by level of renal function, crude ORs were reported. Mantel–Haenszel common OR estimates were used where appropriate to adjust for potential confounders such as age and/or gender between comorbidity and eGFR. Achievement of target BP was based on the most recent recorded value. To assess the relationship between Hb and GFR in the study population, univariate analysis was performed. Confounders were added into a stepwise multivariate model, assessing their effect on Hb by eGFR.

To calculate the total UK expected number of patients to have anemia as defined by Kidney Dialysis Outcomes Quality Initiative, we multiplied the sum of the total age-standardized expected CKD rates for males and females by the percentage of CKD individuals fitting the KDOQI definition for anemia.

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